

**CLAIMS**

1. A method for improving the specificity of a ligation reaction carried out between a first double stranded polynucleotide having a single stranded portion and a second polynucleotide having a complementary single stranded  
5 portion, said second polynucleotide being present in a sample comprising a mixture of different polynucleotides, comprising:

contacting the sample, under hybridising conditions, with the first polynucleotide and one or more third polynucleotide(s), wherein the third polynucleotide(s) comprises a single stranded portion that differs from the single  
10 stranded portion of the first polynucleotide by at least one base substitution, and carrying out a ligation reaction.

2. A method according to claim 1, wherein the third polynucleotide is a double stranded polynucleotide having said single stranded portion.

3. A method according to claim 1 or claim 2, wherein the single  
15 stranded portion on each of the first, second and third polynucleotides is from 3 to 6 bases in length.

4. A method according to claim 3, wherein the single stranded portion is 4 bases in length.

5. A method according to any preceding claim, wherein the single  
20 stranded portion of the third polynucleotide differs from the single stranded portion of the first polynucleotide by one base.

6. A method according to any preceding claim, wherein the ligase is T4 DNA ligase.